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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/121,798 | 07/23/1998 | ROBERT BRIDENBAUGH | 018484-00120 | 3701 |

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EXAMINER

VOGEL, NANCY S

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1636

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/121,798

Applicant(s)

BRIDENBAUGH ET AL.

Examiner

Nancy T. Vogel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-26 and 28-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-26, 28-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Claims 23-43 are pending in the case.

Receipt of the terminal disclaimer, amendment, and arguments on 6/11/04 is acknowledged.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 23-26, 28-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nochumson et al. (US Patent Appl. 2001/0034435 A1) in view of Wan et al. (US 5,837,529), Lee et al. (US Patent 6,197,553), and Song et al. (J. Chem. Soc. Faraday Trans. 1995, 91 (19), 3389-3398) (all of record).

This rejection is maintained essentially for the reasons made of record in the previous office action mailed 2/11/04, modified to include claims which have been amended in the response from applicants on 6/11/04 (claims 23-26 and 28), and to include claims which were omitted from the previous statement of the rejection through typographical error (28-36, 42, 43).

Nochumson et al. disclose a method for purifying plasmid DNA comprising: a) lysing cells with alkaline conditions, b) removal of precipitated proteins, chromosomal DNA and cell debris (paragraphs 0049, 0074-0075), c) filtration (paragraph 0076), d) contacting a solution comprising plasmid DNA with a trimethylamino ethyl (TMAE) anion exchange chromatography resin, the solution having a conductivity at which the plasmid DNA is bound to the resin e)

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washing the resin and f) eluting the plasmid DNA with a step or continuous gradient of increasing conductivity (paragraph 0077) g) ultrafiltration/diafiltration followed by sterile filtration (paragraph 0079) (see page 4, paragraphs 0041 – 0045, Fig. 3, page 6, paragraphs 0074-0080, claims 18-27.). The reference discloses that the lysis solution and precipitation/neutralization solution is mixed with the cells by flowing through in-line static mixers (paragraph 0084).

The difference between the reference and the claims is that the reference does not disclose the use of at least one glass fiber filter and at least one nylon filter prior to anion exchange chromatography, RNase is not used, and the step of purifying used ultrafiltration in the presence of a gel layer is not specified.

However, Lee et al. disclose a method of plasmid purification in which RNase is used to eliminate RNA prior to filtration and anion exchange purification (paragraph bridging col. 2-3). Two filtration steps of the lysate are disclosed (col. 7, lines 5-10). Wan et al. disclose a method for purifying large quantities of plasmid DNA for pharmaceutical use by mixing a solution of bacterial cells comprising plasmid DNA with an alkaline lysis solution by flowing through a first static mixer to obtain a lysate, and contacting the lysate with a precipitating solution by flowing through a second static mixer, thereby forming a precipitation mixture (see abstract, figures, and col. 2-4). The precipitation solution is potassium acetate (col. 4, line 23-24), and the lysing solution is alkaline (col. 4, lines 17-19). Wan et al. disclose filtering the lysate through membrane filter to remove insoluble materials, and subjecting the filtrate to ultrafiltration to remove impurities (see col. 1, lines 42-54). The reference discloses that the material of

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the membrane filter may be any commercially available filter, preferably with a pore size of 0.1-0.2 μm . (col. 2, lines 38-46). Song et al. disclose that the process of ultrafiltration involves the development of a polarization layer of the solute on the ultrafiltration membrane, which provides a resistance to flow through the ultra filter. The presence of this layer provides a gel layer through which all other solute must pass (see page 3390, col. 2, Figs. 1 and 2, and page 3394, col. 1, and discussion at page 3396, col. 2) .

It would have been obvious to one of ordinary skill in the art at the time of filing of the instant application to combine the method for purifying plasmid DNA from such impurities as endotoxin, with the steps from methods for purifying plasmid DNA disclosed by Wan et al. and Lee et al., because they were all involved in the process of purifying large quantities of plasmid DNA for pharmaceutical use. One would have been motivated to do so by the disclosed advantages of such steps as RNase treatment (removal of RNA molecules, an impurity), filtration (removal of debris impurities), and ultrafiltration (removal of impurities). Song et al. provides the theoretical background teaching that a gel layer would be present in an ultrafiltration process.

Applicants have argued in their response received 6/11/04, that "none of the cited references, alone or in combination, teach or suggest the use of filtration through at least one glass filter and at least one nylon filter in plasmid purification, much less the further combination with alkaline lysis through static mixers and TMAE anion exchange chromatography" (page 13 of the response). However, as was set forth in the previous Office action, Nochumsom et al.

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disclose a method of plasmid purification comprising alkaline lysis of cells, followed by removal of precipitated debris, filtration, TMAE anion exchange chromatography. While the reference does not explicitly disclose the use of glass fiber filter and nylon filters in the disclosed filtration step, the other cited references (Lee et al. and Wan et al.) disclose methods of plasmid purification using any commercially available membrane filters having a small pore size, which would include glass or nylon filters (col. 5, lines 27-34). Furthermore, Nochumsom et al. disclose that after alkaline lysis, centrifugation and filtration is performed, and the reference states that "These also are well known techniques that may be performed in a variety of ways known to those skilled in the art" ([0067], at page 6). Therefore, such filtration to remove debris and contaminants was a well known step in plasmid purification, as disclosed by the references. Therefore, applicant's arguments have not been found to be convincing, and the rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is

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filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


TERRY MCKELVEY
PRIMARY EXAMINER